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REMARKS

Prior to this amendment claims 14-34 were pending. Claims 14, 21, 23 and 24 have been amended. Support for the amendments to claims 14 and 23 can be found throughout the specification, *e.g.*, page 9, lines 26-28, in the claims as filed and at page 15. Claim 24 was amended for clarity. Claims 35-39 are new. Support for new claims 35, 36 and 37 find support in claims 14, 21 and 24, respectively, as filed, at p. 19, lines 4-6, and at p. 15, lines 24-25. Support for new claims 38-39 is found throughout the specification including p. 16, lines 27-29, p. 4, line 15 and figure 1. No new matter has been added by way of these amendments. Thus, entry of these amendments is respectfully requested.

Rejection under 35 U.S.C. § 112

Claims 21, 22, 27, 28, 33-34 stand rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Specifically, the Office contends that Claim 21 is drawn to a method of genotyping, but does not recite method steps of genotyping, so it is unclear whether the steps achieve the claimed method. Applicants traverse the rejection.

Nevertheless, in order to further prosecution of this application Applicants have amended claim 21 to recite "whereby said genotype is determined." Applicants submit

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that it is sufficiently clear from the claims as amended that the method steps achieve genotyping.

Based on the foregoing, Applicants submit that the claim is not indefinite and respectfully requests withdrawal of the rejection.

Rejection under 35 U.S.C. § 102(e) in view of Walt *et al.*

Claims 14, 16, 27, 28, and 30 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Walt *et al.* (U.S. Patent No. 6,327,410, filed September 11, 1998).

Applicants traverse the rejection.

Amended claim 14 is directed to a method comprising providing an array composition comprising a substrate with a surface comprising discrete sites and a population of microspheres comprising at least a first and a second subpopulation, wherein the microspheres of each subpopulation each comprise a plurality of different target analytes, wherein each target analyte is a different molecule and wherein a plurality of the different target analytes are covalently attached to the microsphere, wherein the microspheres are distributed on the surface of the substrate, contacting the array composition with a first set of readout probes and detecting the presence of a first target analyte.

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Walt is directed to a microsphere-based analytic chemistry system. Walt teaches the use of at least first and second subpopulation of microspheres distributed on the surface of a substrate wherein each subpopulation comprises a bioactive agent and an optical signature capable of identifying the bioactive agent.

As the Examiner is aware, anticipation of a claim requires that the reference teach every element of the claims. See M.P.E.P. § 2131. Thus, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See *Verdeegal Bros. v. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). It is imperative that the "identical invention be shown in complete detail as contained in the claim." See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

The Examiner seems to suggest that Walt anticipates the instant claims because Walt teaches hybridization of labeled nucleic acid to the bioactive agent on the microspheres and that this hybridization complex constitutes a plurality of target analytes on the microsphere. However, the claims as amended recite that the microspheres in each subpopulation of the instant invention have a plurality of different target analytes, wherein a plurality of the different target analytes are covalently attached to the microspheres. Accordingly, Applicants submit that Walt does not anticipate the instant invention since Walt does not teach each and every element of

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claims 14, 16, 27, 28, and 30. Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 102(e) in view of Chee *et al.*

Claims 14-34 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Chee *et al.* (U.S. Patent No. 6,355,431, filed May 20, 1999). Applicants traverse the rejection.

The Examiner's position appears to be that because Chee discloses a "plurality of different target analytes (i.e. capture probe and modified primer)" that such a hybridization complex constitutes a plurality of target analytes on the microsphere. However, the claims as amended recite that the microspheres in each subpopulation of the instant invention have a plurality of different target analytes, wherein a plurality of the different target analytes are covalently attached to the microspheres. The passages relied upon by the Examiner although describing a plurality of different target analytes do not describe a plurality of different target analytes attached covalently to a microsphere. Therefore, Chee does not teach each and every element of claims 14 through 34. Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 102(b) in view of Brenner *et al.*

Claims 14-18, 21-26, 28, 30-34 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Brenner *et al.* (U.S. Patent No. 5,864,719, issued December 8, 1998).

Applicants traverse the rejection.

As noted previously, an anticipating reference must teach each limitation of the claims.

Independent claims 14, 21, and 23 are discussed above. All other claims at issue depend from these three independent claims.

Brenner is directed to a method of tracking, identifying, and/or sorting classes or subpopulations of molecules using attached oligonucleotide tags. Brenner discloses complements of oligonucleotide tags attached to beads. Each bead or area on the array has an identical population of attached tags. See Brenner at column 4, lines 16-27. The polynucleotides have an oligonucleotide tag attached, such that different polynucleotides have different tags. *Id.* at lines 35-37. Upon mixture of polynucleotides with the beads under conditions which permit specific hybridization of the oligonucleotide tags with their respective complements, identical polynucleotides will sort onto particular beads or specific areas of the array. *Id.* at lines 34-46. Each of Brenner's beads have the same target analyte or target sequence attached thereto.

The Office asserts that Brenner teaches a plurality of different target analytes based on Brenner's polynucleotide and oligo tag. However, Brenner's polynucleotide and attached oligo tag are distinguishable from the "plurality of different target analytes" as presently claimed. Brenner teaches polynucleotides with oligo tags which are complementary to oligo tags attached to the beads. Although Brenner teaches, that in

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some cases, the same polynucleotide can have different oligo tags attached, upon attachment to the bead, the population on that given bead comprises the same polynucleotide. See *id.* at column 16, lines 26-30.

Similar to the other cited references and in contrast to the instant application, Brenner does not teach a microsphere having a plurality of different target analytes covalently attached to its surface as claimed in the instant invention. While Brenner teaches hybridization complexes, only one of these molecules in the complex is covalently attached to the microsphere. Accordingly, because Brenner does not teach all the elements of the instant invention, the cited reference is not an anticipatory reference. Applicants respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 103

Claims 19, 20, 27, and 29 stand rejected as being unpatentable over Brenner *et al.* (U.S. Patent No. 5,864,719, issued December 8, 1998) and Walt *et al.* (U.S. Patent No. 6,327,410, filed September 11, 1998). The Office's position seems to be that it would have been obvious to the skilled artisan to combine the teachings of Walt and Brenner as to render the instant claims unpatentable. Applicants traverse the rejection.

Claims 19 and 20 depend on claim 14. Claims 27 and 29 depend on claims 14, 21, and 23. All of these claims, as well as cited references Walt and Brenner, have been discussed above.

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To establish a *prima facie* case, three basic criteria must be met. First, the prior art must provide one of ordinary skill in the art with a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or to combine their teachings. See *WMS Gaming Inc. v. Int'l Game Tech.*, 51 USPQ2d 1385, 1397 (Fed. Cir. 1999). The mere fact that references can be modified or combined does not render the resulting modification or combination obvious unless the prior art also suggests the desirability of the modification or combination. See *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990). Second, the prior art must provide one of ordinary skill in the art with a reasonable expectation of success. The skilled artisan, in light of the teachings of the prior art, must have a reasonable expectation that the modification or combination suggested by the Examiner would be successful. See *In re Dow*, 5 USPQ2d 1529 (Fed. Cir. 1988). Third, the prior art, either alone or in combination, must teach or suggest each and every limitation of the rejected claims. The teaching or suggestion to the make the claimed invention, as well as the reasonable expectation of success, must come from the prior art, and not in Applicant's disclosure. See *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). If any one of these criteria is not met, *prima facie* obviousness is not established.

Applicants submit that the combination of the cited references does not render the instant invention obvious. As discussed in the previous sections, neither Walt nor Brenner, when considered independently or in combination, would have taught or

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suggested to one of ordinary skill in the art to make and use the invention as claimed including, for example, making and using an array composition wherein each microsphere in each subpopulation comprises different target analytes/sequences covalently attached to the microsphere. Accordingly, Applicants submit that the cited references taken alone or in combination fail to teach or suggest all of the claim limitations.

In addition, Applicants respectfully remind the Examiner that “[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. MPEP 2141.02 citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). To this end, Applicants submit that Brenner teaches away from the claimed invention. As noted at col. 4, lines 24-28, Brenner clearly teaches that “populations of identical sequences are produced in specific regions. That is, the surface of each support, in the case of a bead, or of each region, in the case of an array, is derivatized by only one type of complement which has a particular sequence.” In contrast, the present claims recite that a plurality of different target analytes are covalently attached to each microsphere. Accordingly, Applicants submit that Brenner teaches away from the claims and therefore is improper reference upon which to base a rejection under 35 USC § 103. As such, a *prima facie* case of obviousness has not been established.

Applicants respectfully request withdrawal of the rejection.

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CONCLUSION

Applicants submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP

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BY: David C. Foster

David C. Foster, Reg. No. 44,685 for
Robin M. Silva, Reg. No. 38,304
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Customer Number: 32940
Dorsey & Whitney LLP
Four Embarcadero Center, Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989
Facsimile: (415) 398-3249